

WHAT IS CLAIMED IS:

1. An instrument for controlling a chemical reaction of reagents comprising: integrated microfabricated elements, said elements including a
5 first reagent chamber for containment of a first one of said reagents, and a means for manipulation of a parameter of said reaction.
2. The instrument of claim 1 wherein said microfabricated elements include a control means for
10 controlling said means for manipulation, and a power source for powering said control means.
3. The instrument of claim 2 wherein said power source comprises a battery.
4. The instrument of claim 1 further including a
15 control means for controlling said means for manipulation, said control means being coupled to said means for manipulation by optical radiation.
5. The instrument of claim 1 further including a control means for controlling said means for
20 manipulation, said control means being coupled to said means for manipulation by electromagnetic radiation.
6. The instrument of claim 1 further including a control means for controlling said means for
25 manipulation, said control means being coupled to said means for manipulation by an electromagnetic field.
7. The instrument of claim 6 wherein said electromagnetic field is substantially comprised of
30 an electric field.

8. The instrument of claim 6 wherein said electromagnetic field is substantially comprised of a magnetic field.

9. The instrument of claim 1 wherein said instrument has an exterior surface, further including an optical window between said first reagent chamber and said exterior surface, whereby exterior light may be directed to contents of said first reagent chamber through said window.

10. The instrument of claim 1 wherein one of said elements comprises a Lamb-wave transducer at a boundary of said first chamber.

11. The instrument of claim 1 wherein said means for manipulation comprises an ultrasound transducer.

12. The instrument of claim 1 wherein said means for manipulation comprises an electromagnetic radiation transducer.

13. The instrument of claim 1 wherein said means for manipulation comprises a means for heating said first chamber.

14. The instrument of claim 13 wherein said means for heating comprises a resistive element near said first chamber.

15. The instrument of claim 14 wherein said resistive element is substantially thermally isolated.

16. The instrument of claim 14 wherein said resistive element is substantially thermally isolated by an envelope of a low-stress material.

17. The instrument of claim 16 wherein a portion of said envelope forms a portion of a wall of said chamber.

18. The instrument of claim 17 wherein said low-
5 stress material is low-stress silicon nitride.

19. The instrument of claim 1 further including a boundary layer forming a wall of said chamber, said boundary layer being comprised of a low-stress material.

10 20. The instrument of claim 19 wherein said low-stress material is low-stress silicon nitride.

21. The instrument of claim 14 further comprising a resonant circuit electrically connected to said resistive element, a means for exciting said resonant
15 circuit at a distance, and a means for monitoring the energy stored in said resonant circuit at a distance, whereby the Q-factor of said resonant circuit may be monitored at a distance, thereby determining the resistance of said resistive element and the
20 temperature of said resistive element.

22. The instrument of claim 13 wherein said means for heating produces a predetermined sequence of temperatures in said first chamber.

23. The instrument of claim 13 wherein said means
25 for heating produces a number of thermal cycles in said first chamber.

24. The instrument of claim 23 wherein said number is greater than ten.

25. The instrument of claim 23 wherein said number is greater than twenty five.

26. The instrument of claim 23 wherein one of said elements comprises a second reagent chamber, and one
5 of said elements comprises a means for pumping said first reagent between said first chamber and said second chamber.

27. The instrument of claim 26 wherein said means for pumping comprises a Lamb-wave transducer.

10 28. The instrument of claim 26 wherein said means for pumping comprises a differential temperature pump.

29. The instrument of claim 1 wherein one of said elements comprises a second reagent chamber, and one
15 of said elements comprises a means for pumping said first reagent between said first chamber and said second chamber.

30. The instrument of claim 29 wherein said means for pumping comprises a Lamb-wave transducer.

20 31. The instrument of claim 1 wherein one of said elements comprises a means for determining the progress of said reaction.

32. The instrument of claim 31 wherein said means for determining comprises a sensor for monitoring the
25 viscosity of one of said reagents.

33. The instrument of claim 32 wherein one of said reagents comprises an intercalating molecule which augments a viscosity change associated with said reaction.

34. The instrument of claim 33 wherein said intercalating molecule intercalates into a deoxyribonucleic acid.
35. The instrument of claim 33 wherein said sensor
5 comprises a flexural wave sensor.
36. The instrument of claim 32 wherein said sensor comprises a flexural wave sensor.
37. The instrument of claim 33 wherein said reagents include a deoxyribonucleic acid.
- 10 38. The instrument of claim 33 wherein said reagents include a ribonucleic acid.
39. The instrument of claim 33 wherein said reagents include a polymer.
40. The instrument of claim 33 wherein said reagents
15 include a large molecule.
41. The instrument of claim 33 wherein said reagents include a protein.
42. The instrument of claim 27 wherein one of said chambers has a capacity of less than a milliliter.
- 20 43. The instrument of claim 27 wherein one of said chambers has a capacity of less than fifty microliters.
44. The instrument of claim 27 wherein one of said chambers has a capacity of less than a microliter.
- 25 45. The instrument of claim 26 wherein one of said chambers has a capacity of less than a picoliter.

46. The instrument of claim 1 wherein one of said elements comprises a means for stirring the contents of said first chamber.

47. The instrument of claim 46 wherein one of said elements comprises a Lamb-wave transducer at a boundary of said chamber, thereby preventing boundary layer effects from reducing the effectiveness of the stirring.

48. The instrument of claim 1 wherein one of said elements comprises an elastomeric window interposed between a boundary of said first reagent chamber and the exterior of said instrument, whereby a second reagent may be inserted into said first chamber by puncturing said window with a hollow needle.

49. The instrument of claim 1 further including a hypodermic needle means for extracting a body fluid, said needle means having a fluid conduit terminating at said first chamber.

50. The instrument of claim 1 wherein said microfabricated elements are formed on a semiconducting substrate.

51. The instrument of claim 50 wherein said semiconducting substrate is composed of a silicon-based material.

52. The instrument of claim 1 wherein said microfabricated elements are formed on a substrate composed of a polymer.

53. The instrument of claim 1 wherein said microfabricated elements are formed on a substrate composed of a glass.

54. The instrument of claim 1 wherein one of said reagents is an organic compound.
55. The instrument of claims 1 wherein one of said reagents is an inorganic compound.
- 5 56. The instrument of claim 1 wherein one of said reagents is a biochemical compound.
57. The instrument of claim 1 wherein one of said reagents is a nucleic acid.
58. The instrument of claim 1 wherein one of said
10 reagents is a protein.
59. The instrument of claim 1 wherein said chemical reaction is a chain reaction.
60. The instrument of claim 59 wherein said chain reaction is a polymerase chain reaction.
- 15 61. The instrument of claim 59 wherein said chain reaction is a ligase chain reaction.
62. The instrument of claim 1 wherein said chemical reaction is comprised of a plurality of substantially similar subreactions.
- 20 63. The instrument of claim 62 wherein said chemical reaction produces a quantity of a target product:
64. The instrument of claim 63 wherein said quantity of said target product increases exponentially with each said subreaction.

65. The instrument of claim 63 wherein said target product increases linearly with each said subreaction.

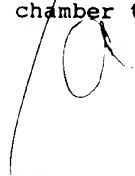
66. The instrument of claim 56 wherein said chemical
5 reaction is a polymerase chain reaction.

67. An instrument for controlling a chemical reaction, said chemical reaction producing a product from a set of reagents, said instrument comprising: integrated microfabricated elements, said elements
10 including an array of chambers for containment of reagents of said reaction, a plurality of channels interconnecting said chambers, and a means for transferring said reagents between said chambers by way of said channels.

15 68. The instrument of claim 67 wherein said elements further include a first heating means for maintaining a first one of said chambers at a first temperature and a second heating means for maintaining a second one of said chambers at a second temperature.

20 69. The instrument of claim 67 wherein said instrument has an exterior surface and further including an optical window between a first selected chamber and said exterior surface.

70. The instrument of claim 68 wherein said means
25 for transferring includes means for repeatedly transferring said reagents located in said first chamber to said second chamber and repeatedly transferring said reagents located in said second chamber to said first chamber.



71. The instrument of claim 67 further including a means for manipulation of a parameter of said reaction.

72. The instrument of claim 67 wherein said chambers
5 in said array are interconnected substantially in series by said channels.

73. The instrument of claim 72 further comprising an input channel and an output channel, a subset of said reagents being continually introduced to said
10 instrument through said input channel, and said product being continually extruded from said instrument through said output channel.

74. The instrument of claim 73 further including a plurality of heaters, said heaters being located
15 proximate said chambers and maintaining said chambers at a plurality of temperatures, whereby transport of said reagents through said chambers subjects said reagents to said plurality of temperatures.

75. The instrument of claim 67 wherein said means
20 for transferring comprises an active pumping means.

76. The instrument of claim 75 wherein said active pumping means comprises a Lamb-wave pump.

77. The instrument of claim 67 wherein said means for transferring comprises a passive pumping means.

25 78. The instrument of claim 77 wherein said passive pumping means comprises a heating means proximate a chamber selected from said array of chambers for heating contents of said selected chamber, whereby said contents may be forced from said selected
30 chamber by heating said contents with said heating

means and thereby increasing the volume of said contents.

79. The instrument of claim 67 wherein said array of chambers is comprised of a plurality of substantially
5 similar groups of chambers.

80. The instrument of claim 79 wherein chambers within a first group are fluidically interconnected, and chambers within said first group are substantially isolated from chambers within a second
10 group. *a*

81. A process for manufacturing on a wafer an instrument for controlling a chemical reaction, comprising the steps of etching said wafer to form a reaction chamber, and depositing a resistive element
15 on said wafer adjacent a boundary of said reaction chamber.

82. The process of claim 81 further comprising the steps of etching a reagent chamber and etching a passage from said reagent chamber to said reaction
20 chamber.

83. The process of claim 81 further comprising the step of depositing a Lamb-wave transducer on said wafer.

84. The process of claim 83 wherein said Lamb-wave
25 transducer is located near a boundary of said reaction chamber.

85. The process of claim 81 further comprising the step of depositing a window of an elastomeric material interposed between a boundary of one of said
30 chambers and the exterior of said wafer.

86. The process of claim 81 wherein said wafer comprises a semiconductor.

87. The process of claim 86 wherein said semiconductor comprises a silicon-based material.

5 88. A microfabricated mixing chamber comprising at least one Lamb-wave transducer for stirring contents of said chamber, thereby preventing boundary layer effects from reducing the effectiveness of the stirring.

10 89. A microfabricated chamber comprising at least one Lamb-wave transducer for viscosity measurements of contents of said chamber, thereby preventing boundary layer effects from reducing the effectiveness of the stirring.

15 90. An instrument for controlling a chemical reaction of reagents comprising: integrated microfabricated elements, said elements including a reagent chamber for containment of a first one of said reagents, said chamber having a first wall
20 and a second wall;

a first Lamb-wave transducer located near said first wall; and

a second Lamb-wave transducer located near said second wall.

25 91. The instrument of claim 90 wherein said first and second walls are located at opposite sides of said chamber.

92. The instrument of claim 91 wherein said first Lamb-wave transducer has two sets of interlaced
30 transduction leads, and said second Lamb-wave

-40- /

transducer has two sets of interlaced transduction
leads. /a

add C1

add
S
D
1